REMARKS

Claims 1-20 are pending and stand rejected.

Miscellaneous

Item 1 of the Office Action indicates that the "continuing data" should be inserted in the specification. The Examiner's attention is respectfully directed to the Preliminary Amendment filed July 1, 2005, wherein the appropriate cross reference was inserted to Page 1 of the specification.

Claim Rejections under 35 U.S.C. §103(a)

Claims 1-20 stand rejected under 35 U.S.C. 103(a) as allegedly being obvious over Harrison, et al., "Combined chemical and mechanical processes for the disruption of bacteria," Bioseparation, Vol. 2, No. 2, 1991, pp. 95-105 ("Harrison") or JP 2001/057895 to Osamu et al. ("Osamu") or EP 0046017 to Walker et al. ("Walker"), or in further view of each other plus further in view of JP 7031487 to Masako ("Masako 1"), JP 7031489 to Masako ("Masako 2"), WO 92/22659 to Kanebo ("Kanebo") or US 6,808,907 to Honma ("Honma"). Applicants respectfully traverse the rejections.

To establish a *prima facie* case of obviousness, the examiner must show that the prior art references themselves or the knowledge generally available to one of ordinary skill in the art would (1) provide some suggestion or motivation to modify or combine reference teachings to obtain the claimed invention, (2) teach or suggest all of the claim limitations, and (3) provide a reasonable expectation that the claimed invention can be made or used successfully. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). *See* M.P.E.P. § 2142. Applicants contends that the Office Action has failed to make a *prima facie* case because the combined teachings of the cited references do not teach or suggest all of the limitations of the claimed invention.

Claim 1 is directed to a method of recovering a polyhydroxyalkanoate from a polyhydroxyalkanoate-containing microbial cell, which includes step (a) of

adding an alkali to an aqueous suspension of the polyhydroxyalkanoate-containing microbial cell ***while*** **stirring and carrying out a physical disruption treatment** to disrupt the cell;

solubilizing or emulsifying cell substances other than the polyhydroxyalkanoate; and

separating the polyhydroxyalkanoate from the aqueous suspension,

wherein the step (a) is followed by a treatment with an enzyme and/or surfactant to solubilize impurities, and then washing the polyhydroxyalkanoate with a hydrophilic solvent and/or water.

Neither Harrison, Osamu, nor Walker discloses all the limitations of claim 1.

Harrison discloses the use of chemical treatments such as alkaline pH shock, addition of a surfactant, or addition of an enzyme as a pretreatment to decrease cell wall strength prior to mechanical breakage by homogenization. See Abstract. and Harrison, page 96, left column, lines 7-13. Harrison discloses that the homogenization is carried out at neutral pH after alkaline pretreatment and neutralization treatment. See, e.g., Harrison, page 96, right column, the last sentences of the first and second full paragraphs; page 98, left column, lines 9-17. According to the Abstract and Table 1, Harrison discloses that **alkali is added before physical disruption**. Harrison differs from claim 1 at least in not disclosing adding an alkali while stirring and carrying out a physical disruption treatment of the cell. In addition, Harraison also differs from claim 1 in that Harrison does not disclose treating with an enzyme and/or surfactant, and then washing with a hydrophilic solvent and/or water after separating the poly-β-hydroxybutyrate from the aqueous suspension as recited in step (b) of claim 1.

The Office Action alleges that Osamu discloses a method of adding an alkali and/or a surfactant to a suspension of microbial cells of PHA-containing microorganism (wherein PHA stands for poly-3-hydroxyalkanoic acid in Osamu). Applicants disagree. Applicants contend that Osamu does not disclose adding any alkali to the suspension of microbial cells. Osamu discloses adding only a divalent or polyvalent metal salt or a surfactant to the suspension of microbial cells. The Office Action cites paragraph [0029] of Osamu as disclosing that the suspension of PHA-containing microbial cells has water as an additive. Applicants note that the suspension of the PHA-containing microbial cells disclosed in paragraph [0029] of Osamu has no water added. The method in paragraph [0029] started with a freeze dried biomass of microbial cells containing PHA without any addition of water. In contrast, paragraphs [0027], [0032] and [0033] of Osamu disclose methods using a suspension of the PHA-containing microbial cells containing some water. The methods of paragraphs [0027], [0032] and [0033] comprise suspending the wet biomass of PHA-containing microbial cells in tetrahydrofuran;

adding calcium chloride (a divalent metal salt) or benzyl trimethylammonium chloride (a cationic surfactant) while stirring; filtering to remove non-dissolved biomass residue; and cooling the filtrate to obtain crystals of 3-hydroxy-butyrate homopolymer. Osamu differs from claim 1 at least in that, in these methods of Osamu, no alkali was added to the aqueous suspension of the PHA-containing microbial cell biomass, let alone adding the alkali to the aqueous suspension while stirring and carrying out a physical disruption treatment to disrupt the cell as recited in step (a) of claim 1. Osamu also differs from claim 1 in not treating the polyhydroxyalkanoate with an enzyme and/or a surfactant, and then washing the polyhydroxyalkanoate with a hydrophilic solvent and/or water as recited in step (b) of claim 1.

Walker discloses a process of recovering PHB, poly(β-hydroxy butyric acid), from PHB-containing bacterial cells by: adding an alkali to an aqueous suspension of the bacterial cells to raise the pH to a value ranging from 8 to 12; adding an acid to the aqueous suspension to reduce the pH to a value ranging from 2 to 5 in order to flocculate the suspension; separating the flocculated cells from the aqueous medium by decanting, filtration, sedimentation, flotation, centrifugation or drying; contacting the flocculated cells with a solvent, such as methanol, in which the lipids associated with the bacterial cell are soluble but in which PHB is insoluble; extracting the PHB from the flocculated cells by contacting the flocculated cells with a solvent in which PHB is soluble; and separating the solvent having the PHB dissolved therein from the cell debris (page 2, line 25 to page 3, line 18; Example 1 in page 5). The Examiner took a position that the decanting is a physical separation. However, applicants note that decanting is not a physical disruption treatment that will disrupt the cells. Walker differs from claim 1 in at least two ways. First, Walker does not disclose adding the alkali while the decanting step is done, let alone adding the alkali while stirring and carrying out the physical disruption treatment to disrupt the cell. Further, Walker discloses the use of decantation as a method of recovery. Unlike the physical disruption treatment used in the present claimed invention, decantation, as disclosed in Walker only renders physical separation. See, e.g., Walker, page 3, lines 23-26. Second, Walker also differs from claim 1 in not disclosing treating with an enzyme and/or surfactant to solubilize impurities as recited in step (b) of claim 1.

Harrison, Osamu or Walker, considered alone, fails to render obvious the claims because there is no suggestion in any one of these references to cure the

deficiencies of each of the particular references as related to step (a) and step (b) recited in claim 1.

Harrison, Osamu and Walker, considered in any combination, also fail to render obvious the claims because there is no suggestion in these references to modify any one of their polyhydroxyalkanoate (PHA) isolation methods to arrive at the claimed method. For instance, there is no suggestion that modifying any one of their PHA isolation methods by treating the aqueous suspension of the PHA-containing microbial cells with an alkali while stirring and conducting a physical disruption treatment to disrupt the cells, and/or by adding a treatment of an enzyme and/or surfactant to solubilize impurities with a reasonable expectation of success.

Applicants further note that the secondary references, Masako1, Masako 2, Kanebo, and Honma are not cited by the Office Action for and do not disclose the step of adding the alkali during the physical disruption treatment, as recited in step (a) of claim 1.

For instance, Masako 1 discloses a method of adding an aqueous NaOH solution to a biomass of PHB-containing microbial cells to form an aqueous suspension; heating at 80°C; centrifuging the suspension; adding methanol and sulfuric acid; and analyzing the PHB content by gas chromatography (see Example 1).

Masako 2 discloses a method of adding an alkali to an aqueous suspension of PHB-containing microbial cells; and then heating and raising the pressure of the aqueous suspension to spout the suspension from a small opening of a container in order to allow the shearing force of the fluid to act on the microbial cells (see Abstract).

Kaneko discloses a method of adding a lytic enzyme to an aqueous suspension of PHA-containing microbial cells to dissolve cell walls; separating and recovering PHA granules in the cytoplasm of the microbial cells, wherein said granules being coated with a granulosa; and removing the granulosa by treating with a protease.

Honma discloses a method of producing purified PHA comprising treating PHA-containing cells with an oxidizing agent to remove cell components other than PHA, wherein the oxidizing agent comprises at least hypochlorite; separating the oxidizing-agent treated cells into a water-soluble fraction and a water-insoluble fraction; and reducing chlorine remained in the water-insoluble fraction (see column 5, lines 11-19).

None of these secondary references provides any teaching or suggestion to modify the methods of Harrison, Osamu and/or Walker to arrive at the methods of claims 1-20, e.g., as related to step (a) and step (b) recited in claim 1, with a reasonable expectation of success. For instance, Masako 1, Masako 2, Kaneko or Honma does not teach (i) treating the aqueous suspension of the microbial cells with the alkali while stirring and conducting the physical disruption treatment to disrupt the cells, and (ii) adding a treatment of an enzyme and/or surfactant to solubilize impurities.

Thus, applicants contend that claims 1-20 would not have been obvious over Harrison, Osamu or Walker, or further in view of each other plus further in view of Masako 1, Masako 2, Kanebo or Honma.

Further, the applicants would like to emphasize the unexpected effect of the present invention. Comparing the present invention with Masako 2, the PHA purity of the claimed invention is higher than that achieved in Masako 2. The purity of the PHB obtained from Masako 2 is 77% and 85.4% as given in Examples 1 and 2. On the contrary, the PHA obtained in the present invention is 96.49% without the treatment of step (b) and is at least 99.62% with the treatment of step (b). See Table I, in page 30, of the specification. One of ordinary skill in the art would not have reasonably expected that the claimed method can obtain PHA with such high purity as compared with the method disclosed in Masako 2.

Withdrawal of the rejection of the claims under 35 U.S.C. §103(a) as being obvious in view of the cited prior art is respectfully requested.

Claim Rejections Under Obviousness-Type Double Patenting

Claims 1-20 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of copending Application No. 10/507,414 to Miyamoto et al in view of the prior art of record. Applicants note that Application No. 10/507,414 has been issued as U.S. Patent No. 7,314,740 (the '740 patent). Without acquiescence with whether the claims in the '740 patent render obvious claims 1-20 in view of the prior art of record, applicants is submitting the enclosed Terminal Disclaimer which renders the Double Patenting rejection moot.

Withdrawal of the obviousness-type double patenting rejection is requested.

Conclusion

It is respectfully submitted that the present application is in a condition for allowance and a notice to that effect is earnestly solicited. In the event that the filing of this paper is deemed not timely, applicants petition for an appropriate extension of time. The Commissioner is authorized to charge Deposit Account No. 11-0600 for the extension of time fee and any additional fees that may be required in relation to this paper.

Respectfully submitted,

KENYON & KENYON LLP

Date: March 7, 2008

King L. Wong

King L. Wong
Reg. No. 37,500

KENYON & KENYON, LLP
1500 K Street, N.W., Suite 700
Washington, D.C. 20005
Tel: (202) 220-4200
Fax: (202) 220-4201